629 General Poster Session, Sat, 8:00 AM - 12:00 PM

A comparative study of exemestane versus anastrozole in post-menopausal breast cancer subjects with visceral disease. *D. A. Cameron, E. Winer, S. Campos, J.-P. Guastalla; Western General Hospital, Edinburgh, United Kingdom; Dana Faber, Boston, MA; Centre Leon Berard, Lyon, France*

Background: A pilot, open-label, multicenter, multinational, randomized, parallel group, comparative study was conducted in post-menopausal women with advanced ER/PgR + breast cancer (BC) and at least one visceral lesion (liver or lung) measurable using RECIST criteria **Methods:** Subjects had progressed during prior antiestrogen treatment, or ≤ 12 months since adjuvant antiestrogen treatment. Subjects were randomized 1:1 to either exemestane (E) (25 mg po qd) or anastrozole (A) (1 mg po qd). Prior treatment with ≤ chemotherapy (CT) regimen for metastatic BC was permitted. ECOG performance status of 0 – 2. Primary efficacy end-point was objective response rate in visceral disease using modified RECIST Guidelines. Stable disease required documentation over 24 weeks. Secondary end-points included tolerability (absence of NCI CTC grade 2 – 4 AEs), TTP, and survival. **Results:** The last patient was enrolled 20Dec2002. 28 patients remained on study drug as of 1Nov2003. Data are shown in the Table. There are no significant differences in efficacy between the two agents; Grade 3 + 4 toxicities of interest looked similar across arms and include hot flashes in 2 (E) and 4 (A) patients, musculoskeletal complaints in 2 (E) and 1 (A). **Conclusions:** On the basis of this study, since 40% of the patients had a response or stable disease for at least 6 months, aromatase inhibitors/inactivators appear to be a suitable choice of therapy for patients with visceral metastatic disease from breast cancer following antiestrogen therapy. The toxicity profile of E and A were similar over the duration of this study treatment.

	Exemestane (n=65)	Anastrozole (n=65)
Median Age (min-max)	61 (43 - 88)	64 (42-84)
Baseline ECOG (0-1)	91%	86%
ER+, PgR+ (%)	ER 94%, PgR 72%	ER 94%, PgR 82%
Sites of visceral disease	Liver 41 (63%)	Liver 36 (55%)
	Lung 38 (58%)	Lung 36 (55%)
	> 3 sites 19 (29%)	> 3 sites 22 (34%)
	Evaluable (n=63)	Evaluable (n=63)
Complete Response (CR)	2	1
Partial Response (PR)	6	12
Clinical Benefit (CR+PR+SD.24 wks)	24 (38%)	29 (46%)
Median TTP (months)	4	4.5

630 General Poster Session, Sat, 8:00 AM - 12:00 PM

A multi-centre phase II trial of pegylated liposomal doxorubicin and trastuzumab in HER-2 over-expressing metastatic breast cancer (MBC). *S. K. Chia, M. Clemons, L. A. Martin, A. Rodgers, K. Gelmon, L. Panasci; British Columbia Cancer Agency, Vancouver, BC, Canada; Toronto Sunnybrook Regional Cancer Centre, Toronto, ON, Canada; British Columbia Cancer Agency, Surrey, BC, Canada; Schering Canada, Montreal, PQ, Canada; Jewish General Hospital, Montreal, PQ, Canada*

Background: Although combination therapy with conventional doxorubicin and trastuzumab (H) improves clinical outcome in HER-2 + MBC, a 27% cardiac dysfunction rate prevents clinical use of this combination. In a large phase III trial in MBC, pegylated liposomal doxorubicin (PLD;Caelyx®) was equally efficacious as conventional doxorubicin, but with significantly less cardiotoxicity. As well, the combination of PLD and H are synergistic in multiple breast cancer cell lines. With this rationale we performed a phase II trial of the combination of PLD and H as 1st line therapy in HER-2 + MBC, with cardiac safety as the primary end-point. **Methods:** Patients with measurable HER-2 + (IHC3+ or FISH positive) MBC were treated with PLD at 50 mg/m^2 every 4 weeks and H at a 4 mg/kg loading then 2 mg/kg weekly. Left ventricular ejection fraction (LVEF) was assessed by MUGA at baseline and after every 2nd cycle. Prior adjuvant anthracycline exposure was allowed. Cardiac toxicity was defined as either a LVEF decline ≥ 15% regardless of absolute value; decline ≤ 10% with absolute LVEF < 45%; or symptomatic congestive heart failure (CHF). **Results:** 30 patients were enrolled from Aug 01 – Sept 03 from 4 Canadian centres. The median age was 59 years (31–75 years). 83% of the patients had visceral metastases, 64% had ER+ tumours and 41% had received prior adjuvant anthracyclines. A median of 6 cycles of PLD has been delivered so far (range 1–9). The mean LVEF at baseline, following cycles 2 and 4 were 63%, 59% and 60% respectively. A total of 3 patients experienced protocol-defined cardiotoxicity. No patient experienced symptomatic CHF. 27% of patients experienced grade 3 palmar-plantar erythrodysesthesia. The response rate (RR) for the evaluable cohort (n=29) was 55%. Within the 17 patients with no prior anthracycline exposure the RR was 65%. Median TTP and OS have not yet been reached. **Conclusions:** The combination of PLD and H is an active combination as 1st line therapy in HER-2 over-expressing MBC, with limited cardiotoxicity. This promising combination warrants further evaluation in the treatment of HER-2 over-expressing breast cancer.

629 General Poster Session, Sat, 8:00 AM - 12:00 PM

New aromatase inhibitors (AIs) as 2nd-line endocrine therapy (ET) in metastatic breast cancer (MBC): A comprehensive review of 5832 women from 14 phase III trials. *P. Carlini, E. Bria, D. Giannarelli, G. Ferretti, P. Papaldo, A. Fabi, E. Ruggeri, M. Milella, E. Terzoli, F. Cognetti; Regina Elena Cancer Institute, Roma, Italy*

Background: New AIs have been developed in controlled clinical trials as tamoxifen failure in MBC. A meta-analysis of the three FDA/EMEA approved AIs revealed that they conferred a significant survival benefit when compared with megestrol (M) *(Messori, Anticancer-Drugs 2000)*. We performed a comprehensive review *(Simes, Stat Med 1987)* including phase-III trials with new AIs (2nd generation - formestane, fadrozole - and 3rd generation - letrozole, anastrozole, vorozole, exemestane) approved or by FDA-EMEA as 2nd-line ET for MBC pts between 1996 and 20 **Methods:** Published or presented trials had to met the following crite phase-III studies evaluating AIs as 2nd-line ET in MBC. No phase-II t were gathered. Letters/editorials, comparative trials of 3rd-generation 3rd-generation AIs or given as adjuvant/neoadjuvant ET were ruled Overall response rate (ORR) and time to progression (TTP) were end-points; survival was excluded because of lack of data. For this anal ratios (HR and RR) and 95% confidence intervals (CI) were der **Results:** Fourteen trials were eligible (5832 pts). No significant differe were seen in the whole group of 9 trials comparing AIs vs M (3908 ORR-RR 1.07, 95% CI 0.88–1.30; TTP-HR 1.00, 95% CI 0.89–1.12 the 6 trials including non-steroidal AIs vs M (2415 pts, ORR-RR 1 95% CI 0.84–1.46; TTP-HR 0.95, 95% CI 0.85–1.07), in the 3 stu comprehending steroidal AIs vs M (1493 pts, ORR-RR 1.08, 95% 0.61–1.94; TTP-HR 1.08, 95% CI 0.61–1.94), in 3 trials comparing generation AIs (letrozole and vorozole) vs 1st and 2 nd generation (aminiglutethimide and fadrazole) (1073 pts, ORR-RR 1.50, 95% 0.78–2.88; TTP-HR 1.18, 95% CI 0.66–2.13), and finally in 2 studies comparing the new AI anastrozole vs the steroidal antiestr fulvestrant (851 pts, ORR-HR 0.86, 95% CI 0.14–1.79; TTP-HR 95% CI 0.07–9.01). **Conclusions:** When all subgroups were analyze ORR and TTP, no significant differences were found. AIs in 2nd-line MBC pts did not seem to add any significant benefit to standard compa arm in terms of ORR and TTP.

631 General Poster Session, Sat, 8:00 AM - 12:

Effect of tandem high-dose chemotherapy (HDC) on long-term co remissions (LTCR) in metastatic breast cancer (MBC), compared to st tional dose (CDC) in patients (pts) who were not selected on the ba response to prior C: Mature results of the IBDIS-I. *J. P. Crown, S. Leyv Verrill, V. Guillem, A. Efremidis, J. Garcia-Conde Bru, R. Welch, A. M R. Leonard, J. Baselga; St. Vincent's University Hosp., Dublin 4, Ir CHUV, Lausanne, Switzerland; Newcastle General, Newcastle, U Kingdom; Duran y Reynals, Barcelona, Spain; St. Savas, Athens, G Clinico Universitario, Valencia, Spain; Christie Hosp., Manchester, U Kingdom; Instituto Catalana de Oncologia, Barcelona, Spain; W General Hospital, Edinburgh, United Kingdom; Vall d'Hebron, Barc Spain*

Background: In single arm studies, HDC (usually single-cycle) wit tograft support appeared to produce an unusually high percentage of in MBC, an observation which was not confirmed in prospective randomi trials (PRT). We have previously reported the results of the pro mandated interim three-year analysis of IBDIS I-a, prematurely termi (post-Bezwoda)PRT of HDC versus CDC in MBC (ASCO 2003). D relatively small numbers (110pts), the primary protocol endpoint free survival (EFS i.e. alive without relapse)-was statistically signifi superior for HDC pts. We now present updated results. **Methods:** PRT without prior CDC for MBC. CDC (mg/m^2): doxorubicin 50/ docetax (AT) x 4 followed by cyclophosphamide / methotrexate/5FU; versus 3xAT followed by tandem autograft-supported HDC (#1-Ifo mide12,000/carboplatin AUC18/etoposide 1200; #2:-cyclophosph 6000/thiotepa 800). The median five year F/U will coincide with 2004, however, as median EFS will still be statistically signifi superior in 6/2004 even if all remaining HDC CR relapse immedia was decided to analyze the data now, at 55 months of F/U. **Results:** intention to treat. The study remains statistically significantly positi median follow-up of 55 months (range 76–30) The median EFS wer 416 and CDC 312 days (EFS: p=0.017 log-rank, RR 0.62). Progre free survivals were: HDC 439, CDC 322 days (RR=0.57; p=.006). were 6 treatment-related deaths on HDC, and 2 on CDC. Six of 56 H are still alive and relapse free (74, 62, 56, 56, 55, 54 months), v CDC patient (49 months). Nineteen HDC pts are alive, versus 1 (median survival 961v 804 days, RR=0.68; p=0.08) Conclusion results do not justify routine HDC, but, given the failure of other treat to produce a meaningful rate of LTCR in this "incurable cancer mandate further study of this approach. IBDIS II will soon be op accrual.

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